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Award Number: W81XWH-04-1-0245

TITLE: Prediction of Aggressive Human Prostate Cancer by Cathepsin B

PRINCIPAL INVESTIGATOR: Akhouri A. Sinha, Ph.D.

CONTRACTING ORGANIZATION: University of Minnesota  
Minneapolis, MN 55455-2070

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14. ABSTRACT I spent considerable effort in several revisions and follow-up discussions with Mr. Peter Marshall and Dr. Julie Wilberding to obtain required approval of the protocols from the HSRRB (Log No. A-12517. The last revision of my protocol (see Feb. 10, 05, letter) met the requirements of the HSRRB (Log No. A-12517). I received approval memo of April 13, 2005 from Col. Laura R. Brosch, Ph.D. that was received around 20th April 2005. Although the grant was funded as of March 1, 2004, I could not conduct any study on human subjects until 4020-05. Earlier, I had sought clarification (March 1, 2004) of the University memo whether I could spend funds to hire personnel. Since Mr. Barry Quast, an experienced scientist, declined to accept the position, this necessitated hiring of new personnel and train them in prostate research. I did receive approval for hiring and spending funds prior to the HSRRB approval (Log No. A-12517). We began utilizing limited amounts of funds after the expiry of the first year (3-1-04 to 2-28-05) of funding. I recruited and hired new employees and trained them in the methods of processing prostatectomy and biopsy tissue samples, immunohistochemical, Elisa assay techniques for cathepsin B and stefin A, and other markers: cytokeratin and prostate specific antigen (PSA) and laser capture microdissection techniques. They also learned methods of acquiring images of reaction products directly from microscopic slides to a computer-equipped with a Metamorph image analysis system, quantitation of localization data, and statistical analysis. The employees are trained in data collection, storage, retrieval, patient confidentiality, <b>Good</b> Laboratory Practices and VHA Privacy Policy. In brief, these employees were trained in the methods required for the study. I began the project as soon as I was given approval by the DOD-HSRRB in April 2005.					
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Annual Report  
March 1, 2004-February 28, 2005  
**Award Number W81XWH-04-1-0245**

Title: Protocol "Prediction of Aggressive Human Prostate Cancer by Cathepsin B,"

Introduction

The first year time period, between March 1, 2004 and February 28, 2005, was spent in obtaining regulatory approvals. The approval was given by the DOD- HSRRB (Log No. A-12517) in April of 2005 and the study began soon after receiving the approval.

Body of the Report

The body of the report outlines the process that required getting approval of the regulatory requirements from the DOD- HSRRB (Log No.A-12517). I contacted Mr. Peter Marshall and Dr. Julie Wilberding many times producing several revisions in the DOD protocol to obtain DOD-HSRRB approval. I received a set of DOD-HSRRB recommendations for revisions from Mr. Marshall in September 14, 2004. This was followed by my response in October 2004 and a point-by-point revision submitted on November 23, 04. I expected DOD-HSRRB approval with each revision. Subsequent discussions with Mr. Marshall indicated that the DOD project ought to be separated from other ongoing studies approved by the VA and University IRBs. This required re-submission of the DOD project to the VA Human Studies Committee and U of MN IRB. I submitted copies of these documents to Mr. Marshall and Dr. Wilberding.

I received a letter from Mr. Marshall (dated Feb 10, 05; I was out of the country until 2-27-05) stating that the revised version was acceptable. I was told, however, that I needed to submit all the documents pertaining to VA Human Subjects Committee's approval as well as approval of the University of Minnesota IRB. I received approval of the University's IRB on 3-31-05. The VA documents were submitted to Mr. Marshall and I received approval of the DOD-HSRRB on 20<sup>th</sup> April, 2005 stating that I could begin the study.

The grant funding began on March 1, 2004, but I was advised in a March 17<sup>th</sup>, 2004 letter by Ms. Karen Sachi of the Sponsored Project Administration of the University of Minnesota that I was not to begin work on the project until the DOD-HSRRB had approved the study. I sought clarification from Mr. Marshall about hiring because I needed to hire and train new technicians for the project. I sought clarification and received a letter from him on April 30, 04 advising me to use funds to hire personnel and purchase supplies. The letter also stated the following restrictions, and I quote, "*none of the funds may be used to recruit or contact potential human subjects, nor review or retrieve any private identifiable human subject information (e.g., medical records) or human anatomical substances.*" Mr. Marshall advised me that I could begin the study only after approval of the DOD-HSRRB Committee.

In the proposal submitted to the DOD, I had requested salaries for Mr. Barry Quast (100%) and Ms. Joan Korkwoski (20%) and for Drs. Ewing (5%), Wilson (5%), and Sinha (25%). Mr. Quast, an experienced and trained scientist (see budget justification), declined to accept the position. I hired Ms. Schwartzhoff and Mr. Buus, 2005, who had no previous experience in the techniques required by the project. Ms. Betre has about two years of experience, but not in the areas suitable for DOD project. I trained these three employees in the appropriate techniques for the successful completion of the DOD work; i.e., immunohistochemistry, Elisa assay, laser capture microdissection, and protocols for data collection, storage, and retrieval. Since I was advised not to recruit or collect human anatomical substances for the DOD project, I could not begin the study. The new employees were trained to collect archival prostate tissue samples using the approved protocols by the VAMC Human Studies Committee and U of M IRB. The samples used in training new employees will not be part of the DOD-supported study. I have, therefore, used funds for training new employees in appropriate techniques without actually conducting the DOD-funded study.

I had been using stefin A antibody from an European Company for about 8 years and it went out of business in December 2004. I located another company, purchased the replacement antibody and validated its use with the help of newly trained employees.

The following civil service employees are paid fringe benefits at the rate of 32.5% year.

Ms. Kongit Betre, BS, was hired at a salary of \$29,120/year starting 5-16-04. She has spent 50% effort on learning techniques for the DOD project.

Ms. Jenifer Schwartzhoff, BS, was hired at a salary of \$26,500/year starting 6-29-04. She has spent 100% effort on learning techniques for the DOD project.

Mr. Ryan Buus, BS, was hired at a salary of \$26,500/year starting 11-01-04. He has spent 50% effort on learning techniques for the DOD project.

#### Key Research Accomplishments:

New personnel were hired and trained so that we could start the study as soon as I received the approvals of the DOD-HSRRB, at which time I began the study on archival prostate tissue samples. I did not waste additional time in hiring and training personnel for the project. I have spent DOD funds wisely and sparingly during the 1<sup>st</sup> year of the project. Because of the delay in starting the study, I may have to extend the completion date of the DOD study at no additional cost to the Agency.

#### The Statement of Work

Task 1: The study could not be initiated due to delay in regulatory approvals.

Task 2: The study could not be initiated due to delay in regulatory approvals.

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Task 3: The study could not be initiated due to delay in regulatory approvals.

Task 4: The study could not be initiated due to delay in regulatory approvals.

Task 5: The study could not be initiated due to delay in regulatory approvals.

Task 6: The study could not be initiated due to delay in regulatory approvals.

Reportable outcome: Techniques for the study were established so that the study could begin immediately after the DOD-HSRRB's approval.

Conclusion: The study could not be started during the first year of funding (March 1, 2004 and February 28, 2005), but the study began in April 2005. Research conducted from April 2005 until now is being submitted in March 1, 2005 and February 28, 2006 report, including manuscript.

If you have additional questions, please contact me.

Akhouri A. Sinha, Ph.D.

Principal Investigator and Professor

And Research Scientist

University of Minnesota and Veterans Affairs Medical Center

Telephone: 612, 467-2846      Fax 612, 725-2093

e-mail: sinha001@tc.umn.edu